UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Offic
Addr ss: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 08/932,834 | 09/18/97 | PORUBEK | D 077319/0129 |

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HM22/0222

| EXAMINER | |
|---|---|
| BERCH, M | |
| **ART UNIT** | **PAPER NUMBER** |
| 1611 | 40 |

**DATE MAILED:** 02/22/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Advisory Action

| Application No. | Applicant(s) |
|---|---|
| 08/932,834 | Porubek |
| **Examiner** | **Group Art Unit** |
| Mark L. Berch | 1611 |

THE PERIOD FOR RESPONSE: [check only a) or b)]

a) ☐ expires _____ months from the mailing date of the final rejection.

b) ☐ expires either three months from the mailing date of the final rejection, or on the mailing date of this Advisory Action, whichever is later. In no event, however, will the statutory period for the response expire later than six months from the date of the final rejection.

Any extension of time must be obtained by filing a petition under 37 CFR 1.136(a), the proposed response and the appropriate fee. The date on which the response, the petition, and the fee have been filed is the date of the response and also the date for the purposes of determining the period of extension and the corresponding amount of the fee. Any extension fee pursuant to 37 CFR 1.17 will be calculated from the date of the originally set shortened statutory period for response or as set forth in b) above.

☐ Appellant's Brief is due two months from the date of the Notice of Appeal filed on _____ (or within any period for response set forth above, whichever is later). See 37 CFR 1.191(d) and 37 CFR 1.192(a).

**Applicant's response to the final rejection, filed on** *Oct 1 and 4, 1999* **has been considered with the following effect, but is NOT deemed to place the application in condition for allowance:**

☒ The proposed amendment(s):

☐ will be entered upon filing of a Notice of Appeal and an Appeal Brief.

☒ will not be entered because:

☒ they raise new issues that would require further consideration and/or search. (See note below).

☐ they raise the issue of new matter. (See note below).

☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal.

☐ they present additional claims without cancelling a corresponding number of finally rejected claims.

NOTE: *See memo*

☐ Applicant's response has overcome the following rejection(s):

☐ Newly proposed or amended claims _____ would be allowable if submitted in a separate, timely filed amendment cancelling the non-allowable claims.

☐ The affidavit, exhibit or request for reconsideration has been considered but does NOT place the application in condition for allowance because:

☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

☒ For purposes of Appeal, the status of the claims is as follows (see attached written explanation, if any):

Claims allowed: _____

Claims objected to: _____

Claims rejected: *1-7 and 9-27*

☐ The proposed drawing correction filed on _____ ☐has ☐has not been approved by the Examiner.

☐ Note the attached Information Disclosure Statement(s), PTO-1449, Paper No(s). _____ .

☐ Other

**MARK L. BERCH**
**PRIMARY EXAMINER**
**ART UNIT 1611**

DETAILED ACTION

The amendment cannot be entered:

1. Applicants have inexplicably changed their mind again about the necessary bond for the formula II structure and removed it again from claims 1 and 20. No explanation was presented as to why this was done. The paper of 7-14-99 had fixed this, as the examiner noted, and that paper is entered, but this paper then seeks to remove it.

2. This paper has versions of claims 21, 23 and 25 which appear to be identical to those presented in the previous paper of 7-14-99, which paper was, as indicated, to be entered. If the claims are identical to those already of record, it is unclear why they were presented again; if the intention was to amend the claims, it is unclear what that change was.

With regard to point 1, the examiner is at a loss to understand why applicants insist on placing the n in the wrong position when it was placed in the right position in the specification (see page 4, structure II). In a chemical formula, a subscripted numeral appears after the thing which it counts. This is a rule without exception. Thus, in $(CH_2)_3$, or $(H_2C)_3$ the 2 counts the number of hydrogens and the 3 counts the number of methylenes, and it appears always after the thing that it counts. Applicants remarks are simply not understood. Applicants refer to "the methyl in formula II" and "$_n(H_3C)$-", but no such groups appear in formula II. The only methyl is at the right side of the formula. Applicants remarks seem to focus on whether the H is placed to

the left or the right of the carbon, but this is completely immaterial. The H can be placed to the left or the right of the Carbon, but the counting numbers must be subscripted after what they count.

With regard to point 3, this is not a new issue. It is the same as point 3 in the Final Rejection which refers back to point 10 in the paper of 4/24/98. With regard to the carbohydrate moiety, the 4/24/98 rejection asked, "What is its structure? How is it formed?" The same question is posed in the most recent Advisory Action, saying, " it is still not seen what these would look like. Applicants are urged to draw out what this would look like for e.g. glyceraldehydyl." The answer which applicants provide makes no logical sense. Yes, the named groups are alcohols. Yes, alcohols can react with acids to form esters, but there is no acid present to react these alcohols with to form an ester. Again, applicants are urged to draw out what this would look like for e.g. glyceraldehydyl. Applicants inability to actually draw out what this will look like is clear evidence that the term is indefinite. Applicants state that "the ethers postulated by the Examiner are not recited." The problem is, if you connect the carbohydrate (denoted as ROH) via its alcohol to the C*H carbon, you get H C*OR, which is an ether, which is exactly what applicants say is not the group formed. The attachment is noted, but the examiner is unable to determine the point of this. It shows that certain powerful oxidants can convert an alcohol into an acid. To begin with, it is not at all clear that the rest of the molecule would survive reagents such as Chromium trioxide, periodates, etc. But even if so, what is the point? To get an ether, you must react an

alcohol with an acid. The carbohydrates have no acid. If these alcohols were converted to their acid form, there would be acid but no alcohol. How will that help? Hence, this is indefinite.

With regard to the enablement rejection, applicants appear to be arguing against assertions which the examiner has not actually made. Thus, applicants state, "Contrary to the assertion of the Examiner, this does not prove that LSF is not good for anything." The examiner said nothing of the sort. The examiner did not say, "LSF is not good for anything". What the examiner said was that the declaration was not credible because the conclusion of the declarant was " directly contradicted by the reference itself". The examiner noted that " last paragraph of the abstract says that lysofylline "did not alter the toxicities of high dose i.v. IL-2 sufficiently to impact the overall dose density of IL-2." and " page 570 says, "Specifically, LSF did not permit the administration of more IL-2 and did not substantially alter the toxicity of a fixed dose of IL-2." Moreover, this failure was not a fluke. Page 571 notes that "Other clinical studies attempting to modify the toxicities mediated by IL-2 and other inflammatory cytokines have also been disappointing." Indeed, the paragraph bridging columns of page 571 strongly suggests that the goal may not be achievable at all" and other remarks. There was, applicants' remarks quote, "the lack of toxicity modulation by LSF." Now, it may be, as the remarks speculate, "that the dose adjusting is required." But the declaration says that the test "bore out its therapeutic usefulness." The test did NOT bear out its therapeutic usefulness; it did the opposite,

it fails to demonstrate "toxicity modulation by LSF." That doesn't mean that LSF is useless. It does mean that 1) declarant's statement that the test "bore out its therapeutic usefulness." is not credible because it is contradicted by the reference and 2) even after all these years of work on LSF, one of ordinary skill in the art still has not been able to figure out how to get it to work. Thus, it wasn't even enabled at the time of the Margolin paper, let alone as of the filing date of this case in 1994.

Applicants refer to Appendices C, D, and E. These were not "ignored." They were discussed in the paragraph bridging pages 4-5 of the previous office action. Applicants now state, "Appendix E demonstrates statistically significant reduction...." but this abstract in fact does not come to any conclusion at all.

Further, the examiner must point out that APPENDIX B (second), C, D or E were not included on the PTO 892 as there is not enough information to cite these and hence these are not of record. Further, the attachment to the paper of 10/4/99 is also not of record. It is impossible to tell what journal or book this came from and hence cannot be cited.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Mark L. Berch whose telephone number is 703-308-4718.

Mark L. Berch

Primary Examiner

Group 1610 - Art Unit 1611

February 14, 2000